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EXAMINER	
CHANDRA, GYAN	
ART UNIT	PAPER NUMBER
1646	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,107	DE LUCA, GIAMPIERO	
	Examiner	Art Unit	
	GYAN CHANDRA	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *1/24/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *18-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/19/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group 1 (claims 1-17) and species sulfonyl urea in the reply filed on 1/24/2008 is acknowledged. The traversal is on the ground(s) that the reference WO 00/23097 does not implicitly teach treating abnormal lipid distribution because hypercholesterolemia may be a clinical manifestation of an abnormal lipid distribution disorder but it is not lipid distribution disorder like lipodystrophy or obesity. This is not found persuasive because the specification does not define the term "abnormal lipid distribution" and because claim 10 recites “elevated level of cholesterol (which is also known as hypercholesterolemia) as an abnormal lipid distribution disorder”. Additionally, regardless of the relationship between hypercholesterolemia and abnormal lipid distribution, the fact remains that the claimed composition is still taught by the prior art, and therefore, no special technical feature exists. However, upon further consideration of search results, the species election requirement has been withdrawn.

The requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, And/Or Claims

Claims 1-24 are pending.

Claims 18-24 are withdrawn from further consideration as being drawn to a nonelected Invention (i.e., Group 2). It is noted that claims 21-24 were inadvertently missed from group II in the previous restriction.

Claims 1-17 are under examination.

Information Disclosure Statement

The IDS filed on 7/19/2007 has been considered.

Claim Objections

The Examiner suggests that syntax of claim 1 can be improved by deleting the term "a human suffering from" because the method is drawn to treating a disease rather than treating a human suffering.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Rudling et al (IDS, WO 00/23097).

Claims 1-8 are broadly drawn to a method of treating an abnormal lipid distribution disorder comprising administering to a human having said disorder a growth hormone and a statin-based therapeutic agent (claim 1), wherein statin-based agent and said growth hormone is provided in a single pharmaceutical composition (claim 2), wherein said statin-based agent is provided in a first pharmaceutical composition and

said growth hormone is provided in a second pharmaceutical composition (claim 3), wherein said growth hormone is recombinant growth hormone (claim 4), wherein said growth hormone is isolated from an animal (claim 5), wherein said statin-based agent is a lovastatin or a lovastatin analog (claim 6), wherein said statin-based agent is selected from the group consisting of atorvastatin, pravastatin, simvastatin, lovastatin, and fluvastatin (claim 7) and wherein said abnormal lipid distribution disorder is non-HIV-related lipodystrophy (claim 8).

Rudling et al teach administering compounds selected from GH, analogues thereof, optionally in combination with established lipid-lowering treatment to mammals with high plasma cholesterol (page 4, 1st paragraph and Detailed description of the invention and claim 1). They teach that the type of GH can be natural (which meets the limitation "isolated from an animal as evident in claim 5") or recombinant, a variant molecule or an analogue thereof (page 4, middle of 3rd paragraph). They teach that a lipid lowering drug can be statins (e.g., atorvastatin, cerivastatin, fluvastatin, pravastatin and simvastatin), and bile acid sequestrants such as cholestyramine (page 5, lines 1-5). The skill of art of substituting one statin with another is well known and therefore, atorvastastatin is being considered an analog of lovastatin (see Scharnragl et al (Biochem. Pharm. 62: 1545-1555). It is noted that the reference Scharnragl et al is not applied as a prior art, but to state the skill of the art. They contemplate using a composition GH, cholestyramine, atorvastatin and combinations thereof, which meets the limitation of claims 2 and 3 (page 6, lines 4-5). Further, the skill of the art of administering pharmaceutical preparations of two compounds separately or in

combination to a subject is well known. Rudling et al contemplate administering a combination therapy to treat hypercholesterolemia in mammals which meets the limitation of claim 8 because they do not explicitly teach that said mammals have HIV. Rudling et al teach using a pharmaceutical composition according to well-established protocols from producer of these drugs (e.g., human GH from Pharmacia and Upjohn and Lipitor (atorvastatin) from Park-Davies) (pages 5-6). Therefore, the prior art of record explicitly or implicitly teaches all the limitations of the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rudling et al (IDS, WO 00/23097) as applied to claims 1-8 above, and further in view of Carr (IDS, AIDS, vol. 17: S141-S148, 2003).

The instant claims are drawn to a method of treating an abnormal lipid distribution disorder comprising administering to a human having said disorder a growth hormone and a statin-based therapeutic agent, wherein said abnormal lipid distribution disorder is an HIV-related abnormal lipid distribution, wherein said HIV-related abnormal

lipid distribution disorder is selected from the atherogenic dyslipidemia, hypertriglyceridemia, elevated levels of cholesterol, elevated levels of LDL cholesterol, and low level of HDL cholesterol, wherein said subject manifests a symptom associated with diabetes related adiposity, wherein said symptom is selected from the group consisting of insulin resistance, beta-cell dysfunction (claim 12), and wherein said subject is suffering from Type 2 diabetes (claim 13).

The teaching of Rudling et al is discussed above. Even though Rudling et al teach treating an abnormal lipid distribution by administering a combination of human GH and a statin, the cited art does not teach treating an HIV-related dystrophy abnormal lipid distribution disorder and wherein said HIV-related abnormal lipid distribution is selected from the atherogenic dyslipidemia, hypertriglyceridemia, elevated levels of cholesterol, elevated levels of LDL cholesterol, and low level of HDL cholesterol, wherein said subject manifests a symptom associated with diabetes related adiposity, wherein said symptom is selected from the group consisting of insulin resistance, beta-cell dysfunction, and wherein said subject is suffering from Type 2 diabetes.

Carr teaches that HIV-infected patients suffering from hypertriglyceridemia, hypercholesterolemia, low-level of HDL cholesterol and insulin resistance (page S141, right column). Carr teaches that the development of type 2 diabetes involves both insulin resistance and impaired insulin secretion (page S142, left column). Carr teaches that retonavir therapy in an HIV-uninfected adult results in abnormal lipid distribution such as increased level in cholesterol, triglycerides and lipoprotein(s) (S143, right column). Carr teaches that HIV infected patients when treated with indinavir result in

rapid onset of insulin resistance (S143, right column). Carr teaches that the administration of growth hormone subcutaneously can reduce intra-abdominal adiposity and buffalo humps (S146, left column). Carr teaches using lipid lowering drugs such as atorvastatin or pravastatin for treating an abnormal lipid distribution and that one of the skill in the art would be able to treat diabetes related symptom (i.e., insulin resistance) by using a drug such as metformin which improves insulin sensitivity (S 146, last paragraph of left column) which meets the limitation of "an insulin secretagogue".

It would have been prima facie obvious to the person of ordinary skill in the art at the time the invention was made to treat an HIV-related subject with a combination therapy using GH and a statin because Carr teaches that said patient comprise high plasma cholesterol, high LDL or low HDL. Further, it would have been obvious to combine an anti-diabetic agent such as metformin with a combination of GH and statin to treat an HIV-related subject having type 2 diabetes and having abnormal lipid distribution because Carr et al teach that insulin resistance which develops in HIV-related patients is treatable by metformin (an insulin sensitizer). The person of ordinary skill in the art would have been motivated do so to treat an HIV-related subject with a combination therapy taught by Rudling et al because an HIV-related subject comprises high plasma cholesterol, low HDL and other abnormal lipid distribution as taught by Carr. One would have a reasonable expectation of success in treating an HIV-related abnormal lipid distribution because Karr teaches that an HIV-related abnormal lipid distribution comprise high plasma cholesterol, high LDL or low HDL which is treatable by administering GH in combination with a statin as taught by Rudling et al. Further, one

would have a reasonable expectation of success in treating an HIV-related subject having type 2 diabetes and having abnormal lipid distribution by a combination of metformin with GH and a statin because treating type 2 diabetic patients have been well in the art. Therefore, the instant invention would have been prima facie obvious to one of the skill in the art.

Claims 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rudling et al in view of Carr et al as applied to claims 1-13 above, and further in view of Van Gaal and Leeuw (Diabetologia, 46: M44-M50, 2003).

The instant claims are drawn to a method of treating an abnormal lipid distribution disorder comprising administering to a human having said disorder a growth hormone and a statin-based therapeutic agent, wherein said subject is further treated with an insulin secretagogue (claim 14), wherein a secretagogue is selected from the group consisting of sulfonyl urea, glyburide....., and exendin-4 (claim 15), and wherein said insulin secretagogue is a non-glucose dependent insulin secretagogue and wherein administering said GH, statin and insulin secretagogue produces insulin release patterns capable of attaining glucose dependent, bi-phasic release characteristics with reduced likelihood of producing hypoglycemia (claim 16).

The teaching of Rudling et al and Carr are discussed above. Even though Rudling et al in combination with Carr et al teach treating an abnormal lipid distribution by administering a combination of human GH and a statin to a human where said subject manifests a symptom associated with diabetes related adiposity, the cited

references do not teach further administering an insulin secretagogue in combination to GH and a statin that produces bi-phasic release characteristic with reduced likelihood of producing hypoglycemia.

Van Gaal and Leeuw teach a combination therapy for type 2 diabetes. They teach a number of insulin secretagogues such as sulfonylurea, repaglinide and nateglinide which enhance insulin secretion and do not have an immediate effect on mealtime glucose excursion (page M47, New approaches to combination therapy). Further, they teach that Nateglinide and repaglinide have dual mode of action; (a) stimulation of insulin release and (b) reduction of postprandial hyperglycemia (this meets the limitation "bi-phasic release characteristic with reduced likelihood of producing hypoglycemia") and teach that their mode of action is complementary to agents that target insulin resistance (page M47, right column). Thus, the secretagogue works in a non-glucose dependent manner.

Therefore, it would have been prima facie obvious to the person of ordinary skill in the art at the time the invention was made to further combine a secretagogue such as sulfonylurea, repaglinide or nateglinide in combination with GH and a statin to treat an abnormal lipid distribution in a subject, since Van Gaal and Leeuw teach using a secretagogue reduces triglyceride and increases insulin secretion which is a desired outcome in said subject. The person of ordinary skill in the art would have been motivated do so because Van Gaal and Leeuw teach that insulin secretagogues are effective in treating insulin resistance and hyepertriglyceridemia. One would have a reasonable expectation of success in further treating a subject having abnormal lipid

distribution and under treatment with GH and a statin with an insulin secretagogue because such agents are being used routinely in the art to control insulin resistance and hypertriglyceridemia in subjects with an abnormal lipid distribution.

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rudling et al (IDS, WO 00/23097) as applied to claims 1-8 above, and further in view of Oral et al (N. Eng. J. Med. 346: 570-578. 2002).

The instant claims are drawn to a method of treating an abnormal lipid distribution disorder comprising administering to a human having said disorder a growth hormone and a statin-based therapeutic agent, wherein said subject is further treated with leptin.

The teaching of Rudling et al is discussed above. Even though Rudling et al teach treating an abnormal lipid distribution by administering a combination of human GH and a statin to a human, the cited art does not teach further administering leptin to said subject. Oral et al teach administering leptin for treating lipodystrophy.

Oral et al teach that lipodystrophy is caused by a deficiency or destruction of adipose cells and which results in conditions including hypertriglyceridemia and insulin resistance (page 570, right column). Oral et al teaches that the administration of leptin reduces triglyceride and treats lipodystrophy (page 575, Discussion).

Therefore, it would have been prima facie obvious to the person of ordinary skill in the art at the time the invention was made to further combine leptin with human GH and a statin for treating an abnormal lipid distribution disorder comprising administering

to a human as taught by Oral et al. The person of ordinary skill in the art would have been motivated to further administer leptin to a subject being treated with GH and a statin for an abnormal lipid distribution because Oral et al teaches that leptin is effective in treating hypertriglyceridemia and insulin resistance (page 575, Discussion). One would have a reasonable expectation of success in further treating a subject having abnormal lipid distribution and under treatment with GH and a statin with leptin because Oral et al teach that leptin is effective in treating a subject having hypertriglyceridemia and insulin resistance.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GYAN CHANDRA whose telephone number is (571)272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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